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10/561,665

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EXAMINER

HENKEL, DANIELLE B

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/561,665	Applicant(s) AWAZU ET AL.	
	Examiner DANIELLE HENKEL	Art Unit 4112	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☒ Claim(s) 15 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 December 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/15/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Summary

1. This is the initial Office action based on the 10/561665 application filed December 20, 2005.
2. Claims 1-15 are pending and have been fully considered.

Information Disclosure Statement

3. The information disclosure statement filed February 15, 2006 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language, specifically JP 6504997.

Drawings

4. The drawings are objected to because they are not labeled with figure numbers as disclosed in the specification. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must

be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

5. The disclosure is objected to because of the following informalities: paragraph 33 discloses the size of the micro flow channel in units of mm although paragraph 31 specifies the "groove having a width and depth of micrometer scale". Therefore it is assumed that the units used in paragraph 33 and claim 3 as millimeter (mm) are a typographical error and are meant to be micrometer (μm). Appropriate correction of the unit abbreviations is required.

Claim Objections

6. Claim 15 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 3-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 3 is considered indefinite because the limitations of the microchip dimensions are claimed in units of millimeters (mm) when the specification discloses the microchip to be on the micrometer scale (Paragraph 31). Claims 4 and 5 are considered as indefinite because they depend on claim 3 and therefore include the indefinite limitation.
9. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 11 does not provide any steps for carrying out a method of using the device in claim 1. The claim as written refers to a use of the claimed invention rather than a method of its use.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 1-6, and 10-13 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by HARRISON (US 6,900,021).

a. In regards to claim 1, HARRISON discloses a microfluidic device preferably in the form of a chip (Column 5, lines 42-43) (cell microchip) that comprises a main flow path (Column 5, line 36) (microflow channel). The device is obtained from a solid substrate that may comprise a plastic material (Column 5, lines 42 & 58) (plastic substrate).

b. In regards to claim 2, HARRISON discloses the flow passages when viewed in cross-section may be triangular, ellipsoidal (oval), square, rectangular, circular, or any other shape with a cross sectional shape transverse to the path of flow (cross sectional shape thereof) (Column 6, lines 11-14).

c. In regards to claim 3, HARRISON discloses the cross section of the flow passages is from 0.1 micrometer to about 2 mm.

d. In regards to claim 4, HARRISON discloses the microfluidic device has at least two inlet flow paths in fluid intersection (one or more junctions) with the main flow path (Column 5, lines 38-40).

e. In regards to claim 5, HARRISON discloses two inlet flow paths (Figure 1, reference # 8 & 8') (flow channels A and B) in fluid intersection (3 pronged junction) with the main flow path (Figure 1, reference # 10) (flow channel C) (Column 5, lines 38-40).

f. In regards to claim 6, HARRISON discloses a method of observing the effect of a compound or a mixture of compounds on cells in a microfluidic device having a main flow path (Column 2, lines 37-40) (micro flow channel constitutes one measurement system using cells). HARRISON also depicts (Figure 3A) an arrangement for an observation device with multiple main flow paths (multiple measurement systems) on a single chip to allow for simultaneous testing of several compounds on the same type of cell at once (Column 8, lines 45-48). Figure 3B also illustrates multiple microfluidic devices on one chip to allow multiple tests at one time (Column 8, lines 64-65).

g. In regards to claim 10, HARRISON discloses using the described microfluidic device in a method for observing the effect of a compound on a cell (method of measurement using cells) (Column 10, lines 6-7).

h. In regards to claim 11, HARRISON discloses the invention allows real time viewing of the effect of a compound of interest on a living cell (Column 13, lines

10-12) and specifically discloses a method for a calcium influx assay (Example III, Column 17) (biological assay method).

i. In regards to claim 12, HARRISON discloses a methodology for using the microfluidic device previously described and depicted in Figure 1 (Column 10, lines 9-24). The method involves introducing a solution containing specific cells (medium to allow cells to grow or live) into the first flow path (Figure 1, reference # 8) (flow channel A) and a candidate compound (chemical containing solution) into the second flow path (Figure 1, reference #8') (flow channel B). Both the flow paths are in fluid communication with the main flow path (Figure 1, reference #2) (flow channel C into which flow channels A and B are merged, 3-pronged junction). Once flow is initiated the cells are allowed to interact with the candidate compound at the intersection (3-pronged junction) and the effect of the compound on the cells is observed in the detection zone (Figure 1, reference #10) shown as part of the main flow path (flow channel C as zone for assaying chemical action). A specific assaying use of an embodiment of the microfluidic system of HARRISON is disclosed in Example III (Column 17-19). The example is for a method of assaying the influx of calcium into lymphocyte cells (Column 17-19) utilizing a microfluidic system depicted in Figure 8. Lymphocytes were suspended in media and mixed with buffer in the "main channel" (flow channel A filled with media to allow cells to grow or live). An activator of calcium influx is added via channel #4 (flow channel B) to mix with the cells at point "B" (3 pronged junction) where the two channels meet the "waste" channel (flow

channel C). The point "B" also functions as the detection zone (zone for assaying the action) on the "waste" channel.

j. With respect to claim 13, HARRISON discloses that the cells from flow path (Figure 1, reference #8) are allowed to interact with the candidate compound at the intersection of the second inlet flow path (Figure 1, reference #8') and the main flow path (Figure 1, reference #2) (Column 10, lines 16-18). As seen in Figure 1 this point of interaction is a 3-pronged junction of flow paths 8, 8' and 2.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 7 and 14 are rejected under 35 U.S.C. 103(a) as being obvious over HARRISON (US 6,900,021) in view of YON-HIN (US WO99/03684).

a. The limitations of claim 1, 12, and 13 are taught by HARRISON as explained in the above 102 (b) rejection. HARRISON does not disclose the plastic substrate of the microfluidic device to be formed from an epoxy resin. HARRISON also does not disclose a method using the microfluidic device in which cells in a single layer fill one of the flow channels. However, YON-HIN

discloses a microstructure of channels or wells on a substrate that can be made of an epoxy resin. The device YON-HIN discloses also may include a whole cell monolayer for assays.

b. With respect to claim 7, YON-HIN discloses the device may be made of cross-linked epoxy resins or other cross-linked polymers (Page 2, line 20). At the time of the invention, it would have been obvious to one of ordinary skill in the art to modify the microfluidic device of HARRISON to include the plastic substrate being formed of epoxy resin of YON-HIN. The motivation would have been that HARRISON discloses the base and cover of the microfluidic device may comprise a plastic material such as resin materials (Column 5, lines 58-60). As disclosed by YON-HIN using a cross-linked epoxy resin in the substrate allows for solvent resistance when the device is used for chemistry reaction carried out in highly aggressive solvents (Page 2, lines 18-21).

c. With respect to claim 14, YON-HIN discloses an embodiment of the microstructure device in which the structures (flow channels) contain whole cell monolayers (cells grow or live linearly in a single layer) which are used for assays (Page 5, lines 27-29). At the time of the invention, it would have been obvious to one of ordinary skill in the art to modify the microfluidic device of HARRISON to include the cell monolayer of YON-HIN. The motivation would have been that providing a cell monolayer allows for prolonged observation of the chemical effect on cells as they are not being flowed past the detection zone. This is analogous to the method disclosed in HARRISON of using stop flow

mode to stop flow when a single cell had entered the detection zone for observation (Column 18, lines 50-52).

14. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being obvious over HARRISON (US 6,900,021) in view of ALAHAPPERUMA (US 6,472,065).

a. The limitations of claim 1 are taught by HARRISON as explained in the above 102 (b) rejection. HARRISON does not disclose the plastic substrate of the microfluidic device having a specific haze value or light transmittance. However, ALAHAPPERUMA discloses adhesive compositions with comparable values.

b. With respect to claim 8, ALAHAPPERUMA discloses that the term haze refers to a reduction in clarity due to the scattering of light and that with increasing haze there is a reduction in the transparency or diminished light transmittance (Column 3, lines 56-67). ALAHAPPERUMA also discloses a coated sheet of silicon covered with methacrylate copolymer with a haze level of less than 8 as clear (Column 3, lines 34-52) and transparent (Column 4, lines 3-5). Also disclosed by ALAHAPPERUMA is that low haze values are characteristic of materials that may be placed over a surface without significantly obscuring the surface (Column 5, lines 29-31). Therefore at the time of the invention, it would have been obvious to one of ordinary skill in the art to modify the plastic microfluidic device of HARRISON to include the methacrylate coated silicon material with the specific haze values of ALAHAPPERUMA. The motivation

would have been that HARRISON discloses the material of cover and base is transparent to ultraviolet, infra red or visible light (Column 5, lines 63-4). As seen from ALAHAPPERUMA the coated sheets have a low haze value, specifically below 8, which is equivalent to being transparent.

c. With respect to claim 9, ALAHAPPERUMA discloses that transparency is considered as a degree of regular transmission and a property of a material by which objects may be seen clearly through a sheet of (Column 4, lines 3-5).

ALAHAPPERUMA also discloses that transparent materials transmit light without diffusion or scattering (Column 4, lines 6-7). It is also disclosed that a reduction in the transparency of sheets is equivalent to diminished light transmittance through the sheets (Column 3, lines 66-67). ALAHAPPERUMA also discloses that silicon surfaces covered by the methacrylate copolymer film sheets are still clearly viewed when the sheets have a light transmittance registers values greater than 92% (Column 5, lines 57-67). Therefore at the time of the invention, it would have been obvious to one of ordinary skill in the art to modify the plastic microfluidic device of HARRISON to include the silicon coated methacrylate copolymer sheets with specific light transmittance of ALAHAPPERUMA. The motivation would have been that HARRISON discloses the material of cover and base is transparent to ultraviolet, infra red or visible light (Column 5, lines 63-4). As seen from ALAHAPPERUMA the coated sheets have a large light ransmittance value which is equivalent to being transparent.

Conclusion

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

DUBROW (US 6,153,073), PARCE (US 6,274,337), CHOW (US 6,274,089), PARCE (US 7,041,509), BLANKENSTEIN (US 7,138,269), TANAKA (US 7,201,873), and OAKLEY (US 7,276,170) all teach microflow devices comprising a channel with at least one inlet for conducting biological or chemical assays similar to the cell microchip of the claimed invention. IDE (US 3,919,157) teaches a thermoplastic resin composition that has a high transparency similar to that claimed as the cell microchip substrate. SHIEH (US 6,361,958) teaches a biochannel assay with a substrate comprising an epoxy resin similar to the substrate of the invention. ZHAO (US 2002/0122747) teaches a microchip with a light transmittance value above 90% similar to that of the claimed invention.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIELLE HENKEL whose telephone number is (571)270-5505. The examiner can normally be reached on Mon-Thur: 7:30am-5pm, Alternate Fridays: 7:30am-4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Barbara Gilliam can be reached on 571-272-1330. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 4128

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DH

/Barbara L. Gilliam/
Supervisory Patent Examiner, Art Unit 4128